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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: RfD/Peer Review Report of the First and Second Meeting on Ethophenprox.

FROM: George Z. Ghali, PhD G. Ghali 3.8.91
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

TO: Addressees

Attached for your review are draft reports for the RfD/Peer Review of Ethophenprox along with an RfD summary sheet.

I'll appreciate receiving your comments no later than March 18, 1991. If a reply is not received by that time, we will presumethat you concur and have no comments.

Addressees

Penny Fenner-Crisp
William Burnam
Reto Engler
Karl Baetcke
Marcia Van Gemert
Henry Spencer
Gary Burin
Marion Copley
Esther Rinde
Stephen Dapson
Rick Whiting

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM:

SUBJECT: RfD/Peer Review Report of Ethophenprox
CAS No. 80844-07-1
EPA Chem. No. 128965
Caswell File No. 427M

FROM: George Z. Ghali, PhD
Science Analysis and Coordination Branch
Health Effects Division (H7509C)
and
Rick Whiting
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

TO: George LaRocca, PM 15
Registration Division (H7505C)

The Health Effects Division RfD/Peer Review Committee met on June 16, 1990 to evaluate data submitted in support of Ethophenprox registration with particular emphasis on long term toxicity in rodent and non-rodent species, carcinogenicity in two species, and developmental and reproductive toxicity.

Since the chemical has been already classified by the Health Effects Division Carcinogenicity Peer Review Committee as a Group C, possible human carcinogen (May 31, 1989), the RfD/Peer Review Committee felt that there was no need to discuss any material related to the carcinogenicity issue. The Committee considered the chronic toxicity phase of the rat long term feeding study to be acceptable, and recommended minor revisions to the existing data evaluation records of this study. The Committee considered that both developmental toxicity studies in rats and rabbits to be unacceptable, and the reproduction toxicity study in the rat to be acceptable. The Committee recommended minor revisions to the data evaluation records for the developmental and reproductive toxicity studies in the rat.

The Committee recommended that the RfD for this chemical should not be established until the requested revisions to the data evaluation records are made.

A. Individuals in Attendance

1. Peer Review Committee (signature indicates concurrence with the peer review unless otherwise stated).

   Reto Engler

   Karl Baetcke

   Mike Ioannou (Marcia Van Gemert)

   Henry Spencer

   Gary Burin

   Stephen Dapson

   George Ghali

   Rick Whiting

2. Peer Review Members in Absentia (committee members who were unable to attend the discussion; signatures indicate concurrence with the overall conclusions of the committee).

   William Burnam

   Marcia Van Gemert

   Esther Rinde

3. Scientific Reviewer (committee or non-committee members responsible for data presentation; signatures indicate technical accuracy of panel report).

   Beth Doyle

B. Material Reviewed

The material available for review consisted of an RfD summary document and data evaluation records (DER's) of the following studies:

1. Green, O., Heaps, C., Heywood, R. et al.(1987). Ethophenprox (MTC 500) potential tumorigenic and toxic effects in prolonged dietary administration to rats, unpublished report prepared by Huntingdon Research Centre Ltd, report No. MTC 59/85581 dated December 15, 1987, submitted by Zoecon Corporation. EPA Accession No. 404494-07, HED Doc. No. 006852, 006981.

Core Classification: Minimum Data.

Committee's conclusions and recommendations:

Since the chemical has already been classified by the Health effects Division Carcinogenicity Peer Review Committee as Group C, possible human carcinogen, the RfD/Peer Review Committee confined its discussion to the chronic toxicity phase of the study. The Committee considered this phase of the study to be acceptable and recommended some minor revisions to the data evaluation records. The Committee felt that the study meets the Core-Minimum data classification criteria. This study satisfies data requirement 83-1 (one species) of Subdivision F of the Pesticide Assessment Guideline.

2. Green, O., Heaps, C., Heywood, R. et al. (1986). Ethophenprox (MTI 500) potential tumorigenic and toxic effects in prolonged dietary administration to mice, unpublished report prepared by Huntingdon Research Centre, Ltd., report No. MTC 58/85582, dated January 6, 1986, submitted by Zoecon Corporation. EPA Accession No. 404497-09, HED Doc. 006852, 007514.

Core Classification: Minimum Data.

Committee's conclusions and recommendations:

This study has not been discussed since the chemical had been classified as a Group C, possible human carcinogen, by the Health Effects Division Peer Review Committee.

3. Hanling, R.J. (1985). Ethophenprox (MTC 500) toxicity to dogs by repeated dietary administration for 52 weeks followed by recovery period of 8 weeks, unpublished report prepared by Huntingdon Research Centre Ltd, report No. MTC 71/85234 dated October 25, 1985, submitted by Zoecon Corporation. EPA Accession No. 404497-06 HED Doc. No. 006852.

Core Classification: Minimum Data.

Committee's conclusions and recommendations:

The Committee considered the study report and the data evaluation records to be acceptable. The study meets the Core-Minimum data classification criteria. The study satisfies data requirement 83-1 (one species) of Subdivision F of the Pesticide Assessment Guideline.

4. Cozens, D., Hughes, E. W., and Anderson, A. (1985). Effects of ethophenprox (MTI 500) on pregnancy of the rat with rearing to maturation of the F1 generation, unpublished report prepared by Huntingdon Research Centre, Ltd., report No. MTC 64/85422, dated October 28, 1985, submitted by Zoecon Corporation. EPA Accession No. 404497-11, HED Doc. 006852, 008069.

   Core Classification: Minimum data.

   Committee's conclusions and recommendations:

   The Committee noted that maternal NOEL was not achieved in this study. Increased salivation occurred in females at all dose levels. Therefore, the study was reclassified as Core-supplementary data and considered to constitute a data gap for requirement 83-3 (one species) of Subdivision F of the Pesticide Assessment Guideline. The Committee requested that additional data tables be added to the data evaluation records to support the reviewer's conclusions.

5. Bottomley, A., Barton, S., Masters, R., Offer, J., Parker, C., Anderson, A. and Dawe, I. (1985). Effect of ethophenprox MTI 500) on pregnancy of the rabbit, Unpublished report prepared by Huntingdon Research Centre, Ltd. report No. MTC 85(84)85444, dated December 20, 1985 submitted by Zoecon Corporation. EPA Accession No. 404497-12, HED Doc. 006852.

   Core Classification: Supplemental data.

   Committee's conclusions and recommendations:

   The Committee considered the study to be unacceptable. The use of animals from three different sources might have compromised the study and therefore, the study should not be upgraded. The data evaluation records was considered acceptable as presented. This study constitutes a data gap under 83-3 (one species) of Subdivision F of the pesticide Assessment Guideline.

6. Cozens, D., Barton, S., Offer, J., Parker, C. and Anderson, A. (1985). Effect of ethophenprox (MTI 500) on multiple generation in the rat, unpublished report prepared by Huntingdon Research Centre, Ltd., report No. MTC 67/85706, dated October 29, 1985, submitted by Zoecon Corporation. EPA Accession No. 404497-13, HED Doc. 006852.

   Core Classification: Minimum data.

Committee's conclusions and recommendations:

The Committee considered the study to be acceptable. However the Committee recommended that the data evaluation records should be further clarified with respect to the NOEL and LEL. The data evaluation records for this study failed to indicate that the NOEL and LEL of 100 and 700 ppm, respectively, cited on 1 of the data evaluation records were in fact for systemic effects only. No reproductive effects were observed in this study under the testing conditions. The reproductive NOEL for ethophenprox is 4900 ppm (HDT). This study satisfies data requirement 83-4 of Subdivision F of the Pesticide Assessment Guideline.

C. RfD Determination

The Committee decided not to establish an RfD for this chemical until the requested revisions to the data evaluation records are made.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MEMORANDUM:

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: Second RfD/Peer Review Report of Ethophenprox
CAS No. 80844-07-1
EPA Chem. No. 128965
Caswell File No. 427M

FROM: George Z. Ghali, PhD G. Ghali
Science Analysis and Coordination Branch
Health Effects Division (H7509C)
and
Rick Whiting
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

TO: George LaRocca, PM 15
Registration Division (H7505C)

The Health Effects Division RfD/Peer Review Committee, again met on February 12, 1991 to evaluate data submitted in support of Ethophenprox registration in light of additional information provided by the reviewer as requested by the Committee in their meeting of July 17, 1990.

In their meeting of July 17, 1990, the Committee considered the chronic toxicity phase of the rat long term feeding study to be acceptable, and recommended minor revisions to the existing data evaluation records of this study. The Committee considered that both developmental toxicity studies in rats and rabbits to be unacceptable, and the reproduction toxicity study in the rat to be acceptable. The Committee recommended minor revisions to the data evaluation records for the developmental and reproductive toxicity studies in the rat. The Committee recommended that the RfD for this chemical should not be established until the requested revisions to the data evaluation records are made.

In the current meeting, the Committee examined the revised data evaluation records and/or the required addenda to the data evaluation records and concluded that the revised data evaluation records and/or the addenda to the data evaluation records are acceptable.

The RfD for this chemical was determined to be 0.05 mg/kg/day based upon a NOEL of 5 mg/kg/day for increase in pup liver weights at weaning in a 2-generation rat reproduction study, using an uncertainty factor of 100. The RfD summary document was modified to reflect changes made to the data evaluation records.

A. Individuals in Attendance

1. Peer Review Committee Members and Associates (signature indicates concurrence with the peer review unless otherwise stated).

   William Burnam

   Reto Engler

   Karl Baetcke

   Marcia Van Gemert

   Henry Spencer

   Gary Burin

   Stephen Dapson

   George Ghali

   Rick Whiting

2. Peer Review Members in Absentia (committee members who were unable to attend the discussion; signatures indicate concurrence with the overall conclusions of the committee).

   Esther Rinde

3. Scientific Reviewer (committee or non-committee members responsible for data presentation; signatures indicate technical accuracy of panel report).

   Beth Doyle

B. Material Reviewed

The material available for review consisted of an RfD summary document and data evaluation records (DER's) and an addenda (HED Doc. No. 008069) of the following Studies:

1. Green, O., Heaps, C., Heywood, R. et al.(1987). Ethophenprox (MTC 500) potential tumorigenic and toxic effects in prolonged dietary administration to rats, unpublished report prepared by Huntingdon Research Cent

re Ltd, report No. MTC 59/85581 dated December 15, 1987, submitted by Zoecon Corporation. EPA Accession No. 404494-07, HED Doc. No. 006852, 006981.

Revisions to the data evaluation records:

Page 1 of the data evaluation records was revised as recommended by the Committee to better express the NOEL and LEL as follows: "The NOEL for ethophenprox in male rats was 100 ppm. The LEL in male rats was 700 ppm based on increased liver weights at 52 weeks and at terminal sacrifices. The NOEL in female rats was 700 ppm. The LEL in female rats was 4900 ppm based on increased liver weights. Male and female rats fed diet containing 4900 ppm of ethophenprox had increased thyroid follicular cell adenomas and carcinomas.

Committee's conclusions and recommendations:

The Committee found the data evaluation records as revised above to be acceptable. The revision was considered to be a better summarization of the existing data evaluation records and does not constitute changes in the contents of the existing data evaluation records or the classification of the study. The study classification should remain as Core-minimum data.

2. Cozens, D., Hughes, E. W., and Anderson, A. (1985). Effects of ethophenprox (MTI 500) on pregnancy of the rat with rearing to maturation of the F1 generation, unpublished report prepared by Huntingdon Research Centre, Ltd., report No. MTC 64/85422, dated October 28, 1985, submitted by Zoecon Corporation. EPA Accession No. 404497-11, HED Doc. 006852, 008069.

Revisions to the data evaluation records:

The data evaluation records were revised to address the concern expressed by the Committee in the meeting of July 17, 1990 with respect to the NOEL for maternal toxicity. During consideration of this study in the previous meeting, it was noted that no maternal NOEL was achieved since increased salivation occurred in females of all treated groups. Therefore, the study was downgraded by the Committee from Core-minimum to Core-supplementary and constituted a data gap under data requirement 83-3 (one species) of Subdivision F of the Pesticide Assessment Guideline. The Committee also requested at this time that additional tables be included in the data evaluation records to support conclusions made in that report. In the current meeting the reviewer reported to the Committee that the increased salivation was considered

to be a systemic effect rather than a maternal toxic effect. In addition, the reviewer provided tables needed to support conclusions made in the existing data evaluation records of this study (see addendum to the DER, HED Doc. No. 008069).

Committee's conclusions and recommendations:

The Committee considered the data evaluation records as revised to be acceptable. The study was upgraded back to Core-minimum data. The study satisfies data requirement 83-3 of Subdivision F of the Pesticide Assessment Guideline.

3. Cozens, D., Barton, S., Offer, J., Parker, C. and Anderson, A. (1985). Effect of ethophenprox (MTI 500) on multiple generation in the rat, unpublished report prepared by Huntingdon Research Centre, Ltd., report No. MTC 67/85706, dated October 29, 1985, submitted by Zoecon Corporation. EPA Accession No. 404497-13, HED Doc. 006852.

Revisions to the data evaluation records:

In the original review of this study, the data evaluation records failed to accurately specify that the NOEL and LEL of 100 and 700 mg/kg/day, respectively, were in fact for systemic effects only and no reproductive effects were observed in this study. The reproductive NOEL was considered to be 4900 ppm (see HED Doc. No. 008069).

Committee's conclusions and recommendations:

The Committee considered the data evaluation records as revised to be acceptable. The study satisfies data requirement 83-4 of Subdivision F of the Pesticide Assessment Guideline.

C. <u>RfD Determination:</u>

The RfD was determined to be 0.05 mg/kg/day based upon a NOEL of 5 mg/kg/day for increase pup liver weights at weaning in a two generation rat reproduction study, using an uncertainty factor of 100.

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# R057584

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|---|---|
| **Chemical:** | Ethephenprox ~~Gas cartridge (as a device for burrowing~~ |
| **PC Code:** | ~~000000~~ 128965 |
| **HED File Code** | 21200 PEER REVIEW |
| **Memo Date:** | 03/08/91 12:00:00 AM |
| **File ID:** | 00000000 |
| **Accession Number:** | 412-04-0046 |

**HED Records Reference Center**
**03/05/2004**